REMARKS

Claims 1, 5-9. 12, 14, 15, 18-20, 22, -25, and 29 are pending. Applicants have amended claims 1, 5, 12, 15, 18-20, 22-25 and 29.

Claim 1 has been amended to replace the recitation of "heart-specific promoter" to "a promoter that is capable of directing expression of" [the transgen] in the heart of the transgenic mouse. Claim 5 has been amended to become independent, incorporating all elements of the base claim. Claim 29 has been amended to recite that the transgenic mouse develops heart hypertrophy or fibrosis. Other claim amendments are made to obviate assertions of claim indefiniteness. With the exception of claim 29, none of the amendments narrows the scope of the claims. All claim amendments are fully supported by the specification. For example, as will be discussed below in more detail, the Office Action contends that the α-MHC promoter specifically exemplified in the specification is not "heart-specific," and amendment to Claim 1 merely avoids such a "label," but to merely state the function of the promoter. Entry and favorable reconsideration are respectfully requested.

Claim Objections

The Office Action objected to Claims 15, 20, and 22-28 for not using the definite article "the" in the preamble or in referring to the mouse of a previous claim.

As an initial matter, applicants note that Claims 26-28 have been cancelled, and their inclusion in this objection appears to be in error.

With regard to the other claims, applicants continue to respectfully submit that the objection is improper, but in order to expedite prosecution, have amended relevant claims chaining "a" to –the-, with the exception to Claim 23 and 24. In Claims 23 and 24, a similar change would create confusion and indefiniteness, demonstrating the fallacy in the assertion that a claim reciting "a mouse" means there is only one mouse. Reconsideration and withdrawal of this objection are respectfully requested.

Claim Rejections under 35 U.S.C. § 112, ¶ 1

The Office Action rejected all pending claims for alleged lack of enablement. From the lengthy discourse, applicants gather that the rejections are based on the following three grounds: First, transgenic integration and expression are so unpredictable that only the specific mouse described in the application is enabled, but not other mice. Second, the description only enables the use of the alpha myosin heavy chain (α-MHC) promoter, and not other promoters. Moreover, the Examiner alleges that the α-MHC promoter is not a heart specific promoter. Third, only heterozygous, but not homozygous, animals are enabled, because the homozygous mouse could have a lethal phenotype. Applicants respectfully traverse, and provide the reasons for the traversal below accordingly.

First, the law is clear that "[t]he test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation." see *United States v. Telectronics, Inc.*, 857 F.2d 778, 785, 8 USPQ2d 1217, 1223 (Fed. Cir. 1988) (emphasis added). The Office Action is correct that the art of producing transgenic mice may be unpredictable and it may involve a lot of trial-and-error and screening to obtain an animal with the desired phenotype. Significantly, even using the α-MHC promoter and SEQ ID NO: 1 or 2 without using the specific mouse exemplified in the instant specification, a person of ordinary skill in the art of transgenic mouse production will still have to expend a large amount of time and resources to produce a transgenic mouse having the desired phenotype (i.e., a mouse as claimed in Claim 5. This is the type of effort routinely expended in this art. There is no evidence or any basis to assert that simply changing to a different yet similar promoter (many of which are known and readily available to the ordinarily skilled artisan) would require significantly more experimentation that would amount to undue experimentation as required under the case law. In other words, if the examiner considers that the method recited in Claim 5 is enabled, there is no reason to assert that the method recited in Claim 1 is not.

Second, the observation that the α-MHC promoter also expresses in some lung tissue does not diminish the fact that it is a heart-specific promoter, as this term is understood by those skilled in the art. Strictly non-leaking promoters are in fact a rare

thing. In any event, the authors of the Subramaniam *et al.* article, which the examiner cites, themselves use the term "cardiac-specific expression" to describe the specificity of the α-MHC promoter (see e.g. page 24618, left col., seven to last line). Again, in order to expedite prosecution and advance this application to allowance, applicants have amended Claim 1 to avoid using the term "heart-specific" promoter.

Third, the Office Action questions whether homozygous transgenic animals are viable or not. Apparently the Office Action does not argue that making an animal homozygous would involve undue experimentation (because it would not). The Office Action only manifests a doubt as to whether the homozygous transgenic mouse would be lethal or not. This doubt, however, is not a technically sound one, and certainly not a proper legal ground on which to base a rejection under 35 U.S.C. § 112, ¶ 1. Embodiments described in the specification of a patent application are presumed to have been reduced to practice ("constructive reduction to practice") unless there is a reasonable and articulated ground to challenge this legal presumption. In fact, the present inventors have actually made homozygous transgenic animals, and will submit a declaration if demanded by the Office.

In summary, applicants respectfully submit that the above arguments, in combination with the claim amendments, have overcome the claim rejections under 35 U.S.C. § 112, ¶ 1, for the alleged lack of enablement. Withdrawal of the rejections are respectfully requested.

Claim Rejections under 35 U.S.C. § 112, ¶ 2

The Office Action rejected Claims 5, 12, 20, and 22-24 for indefiniteness. Applicants respectfully submit that amendments to these claims have overcome these rejections.

Claim Rejections under 35 U.S.C. § 102 and § 103

The Office Action rejected Claim 12 under 35 U.S.C. § 102(e) over Galvin et al. (U.S. Pat. No. 6,359,194). Applicants respectfully submit that, pursuant to the Examiner's kind suggestion, the claim has been amended and the rejection is overcome.

The Office Action also rejected Claim 29 under 35 U.S.C. § 103 for alleged obviousness. In response, applicants have amended the claim to recite that the transgenic mouse develops heart hypertrophy or fibrosis, which the prior art does not teach or suggest. Accordingly, this rejection has been overcome.

Applicants respectfully submit that all claims are now free of the prior art and are in condition for allowance, and earnestly solicit an early indication to that effect from the Examiner.

If necessary to effect a timely response, this paper should be considered as a petition for an Extension of Time sufficient to effect a timely response, and please charge any deficiency in fees or credit any overpayments to Deposit Account No. 05-1323 (CAM #: 029065.48487US).

Respectfully submitted,

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Kening Li, Ph.D.
Registration No. 44,872
J. D. Evans
Registration No. 26,269

CROWELL & MORING, LLP
Intellectual Property Group
P.O. Box 14300
Washington, DC 20044-4300
Telephone No.: (202) 624-2500
Facsimile No.: (202) 628-8844
JDE:KL:tlm (029065.48487US)